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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,087	12/19/2001	Timothy J Fischer	9250-5CTIP4XX	3082

7590 07/17/2006

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,087	FISCHER ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40,43,45-47,49,52,53,56-65,69 and 70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *52 and 53* is/are allowed.

6)☒ Claim(s) *40,43,45-47,49,56-65,69 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/28/06 has been entered.

2. Claims 40, 43, 45-47, 49, 52-53, 56-65, and 69-70 are pending and are being acted upon in this Office Action.

3. The proposed examiner's amendment communicated to Shawna Cannon Lemon on July 6, 2006 is hereby withdrawn in view of the following issue. Although the claim language has significantly improved over the course of communication and in order to better understand applicants' invention, it is best that applicants' representative schedule an interview with the examiner, at least one of the inventors and applicants' representative to clarify the claimed invention before responding to this Office Action.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 40, 43, 45-47, 49, 56-65, and 69-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method for determining whether or not a patient has hemostatic dysfunction wherein the method comprising obtaining a plasma or serum sample from a patient, measuring the increase in prothrombin (PT), or the increased in activated partial thromboplastin time (APTT) over time by adding divalent metal ion calcium and an anticoagulant, quantitating the amount of precipitate in the sample by measuring the decreasing levels of light transmittance at 18 seconds, and determining the slope wherein an increase in the slope at the later time is indicative of progression of hemostatic dysfunction and wherein a decrease in the slope at the later time is indicative of regression hemostatic dysfunction (see page 5, 13-21 of specification), **does not** reasonably provide enablement for a method of diagnosing or

monitoring hemostatic dysfunction comprising an inflammatory condition as set forth in claims 40, 43, 45-47, 56-65, and 69-70 and a method of testing the effectiveness of a therapeutic as set forth in claim 49. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

Enablement is not commensurate in scope with methods in which adding metal divalent cation *and* CRP or serum amyloid A to a test sample to cause formation of complex of one or more lipoproteins selected from the group consisting of chylomicrons, VLDL, and IDL, and said one or more acute phase protein, then measuring the formation of complex, and correlating the formation of complex to a concentration of one or more lipoproteins that are observed in said patient.

The specification discloses a method for determining whether or not a patient has hemostatic dysfunction by obtaining a plasma or serum sample from a patient, measuring the increase in prothrombin (PT), or the increased in activated partial thromboplastin time (APTT) over time by adding divalent metal ion calcium and an anticoagulant, quantitating the amount of precipitate in the sample by measuring the decreasing levels of light transmittance at 18 seconds or overtime, and determining the slope wherein an increase in the slope at the later time is indicative of progression of hemostatic dysfunction and wherein a decrease in the slope at the later time is indicative of regression hemostatic dysfunction (see page 5, 13-21 of specification). The specification at page 32 further discloses lipoproteins selected from the group consisting of VLDL, IDL and chylomicrons form complex with C-reactive protein (CRP) while VLDL forms complex or precipitates with serum amyloid A (SAA). This is done by adding divalent metal cation calcium to a patient's citrated plasma, detecting the formation of precipitate of CRP forming complexes with lipoprotein VLDL at 18 seconds or overtime to get the slope of the clot

profile (see page 33). The detection of precipitate formation correlates to clinical outcome, patient death (see page 34). Further, the greater the formation of the precipitate at later time (the greater the decrease in transmittance or increase in slope), the greater the predictor of impending death in patient with hemostatic dysfunction associated with inflammatory condition, see page 35 of specification. The specification at page 39 discloses the invention is useful for detecting complex formation in the absence of adding exogenous lipids to the test sample. The invention is for detecting a patient's own lipoproteins such as VLDL complexed with the patient's own acute phase proteins such as CRP as a predictor of clinical outcome.

However, the specification does not teach adding at least one reagent comprising a divalent metal ion and at least one acute phase protein such as C-reactive protein (CRP) or serum amyloid A. In fact, a patient with hemostatic dysfunction associated with inflammatory condition has high level of C-reactive protein. It is not clear adding acute phase protein to the patient's serum sample in addition to calcium could detect a patient's own lipoproteins such as VLDL complexed with the patient's own acute phase proteins such as CRP as a predictor of hemostatic dysfunction associated with an inflammatory condition. Clarification is required.

Further, because the readout of the claimed method is precipitate or complex formation between at least one acute phase protein such as C-reactive protein (CRP) or serum amyloid A and at least one lipoproteins such as VLDL and IDL, simply adding divalent metal ion such as calcium to a patient's serum sample without inhibiting fibrin polymerization (clotting) would appear to interfere with the complex formation in the claimed method for diagnosing or monitoring hemostatic dysfunction associated with an inflammatory condition. In other words, how specific is claimed method for diagnosing hemostatic dysfunction *associated with an inflammatory condition*?

The 6,429,017 patent (of record) teaches precipitate formation is capable of being detected in patients with haemostatic dysfunction when a clotting agent is used, it is beneficial that the reagent used is capable of forming the precipitate *without* fibrin polymerization.

With regard to claim 49, there is insufficient guidance as to which one or more reagents to be added to cause the formation of a complex of any acute phase protein and lipoproteins present in the test sample. Further, the specification discloses only divalent metal ion calcium. The specification does not teach any other metal ion to be used for the claimed method of testing the effectiveness of a therapeutic.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

6. Claims 52-53 are allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

8. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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July 10, 2006

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